Epigenetic regulation of stem cells differentiating along the neural lineage.

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Public Summary:
In this review article, we outline how one of the epigenetic mechanisms, DNA methylation, regulate the proliferation and differentiation of stem cells during development. Intricate relationship between DNA methylation and de-methylation, along with histone modifications, ensures proper division and differentiation of neural stem cells. In addition, DNA methylation on neuronal genes that is distal to transcription start site enable transcription activation, which is different from the classical inhibitory view of DNA promoter methylation. Collectively, the epigenetic machinery instructs neural stem cells to generate neurons and glia in a timely manner to govern proper development of the central nervous system.

Scientific Abstract:
Many lineage-specific genes are poised and silenced in stem cells. Upon differentiation, genes that are related to self-renewal and alternative lineages are stably silenced. CpG methylation at proximal promoters and PRC2-mediated H3K27me3 play a role in silencing genes temporarily or permanently, with or without coexistence of active epigenetic marks, respectively. Interestingly, DNA methylation on neuronal genes that is distal to transcription start site enable transcription activation owing to its ability to repel PRC2-mediated inhibition. In addition, DNA demethylase Tet proteins play a role in regulation of changes in DNA methylation and related H3K27me3 during differentiation. Collectively, a complex epigenetic network formed by H3K4me3, histone acetylation/deacetylation, H3K27me3 and DNA methylation/demethylation act together to regulate stem cell self-renewal and differentiation.